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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/075,918	02/13/2002	Nicole Chantel Barvian	A0000426-01-CFP	9234

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EXAMINER	
OH, TAYLOR V	
ART UNIT	**PAPER NUMBER**
1625	

DATE MAILED: 01/07/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/075,918	BARVIAN ET AL.	
	Examiner	Art Unit	
	Taylor Victor Oh	1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 December 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *3,6,7 and 18-23* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *3, 6, 7, and 18-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Applicant's arguments with respect to claims 3, 6-7, and 18-23 have been considered but are moot in view of the new ground(s) of rejection.

The Status of Claims:

Claims 3, 6-7, and 18-23 are pending.

Claims 3, 6, and 18-23 have been rejected.

Claims 1-2, 4-5, and, 8-17 have been canceled.

Claim 7 has been objected.

DETAILED ACTION

1. Claims 3, 6-7, and 18-23 are under consideration in this Office Action.

Priority

2. Provisional Patent Application number 60/268,736 filed 2/14/2001 has been acknowledged.

Drawings

3. None.

Specification

In the specification on page 4 ,line 10 , a compound of formula III is recited. In the formula, the chemical symbols " R^4R^5—N " and " N —R^4R^5 " are recited. The expression of the bond "— " between the N and the R^4R^5 is improper. The examiner recommends to remove the bond "— " between the N and the R^4R^5.

Appropriate correction is required.

Claim Objections

Claim 7 is objected to because of the following informalities:

In claim 7 , there are duplicate chemical compound names and a triplicate chemical compound name in the claim; the duplicate chemical compound names are **4-Methoxy-isophthalic acid di-2,1,3-benzothiadiazol-5-ylmethyl ester** and **N1,N3-Bis-1,3-benzodioxol-5-ylmethyl-4-isopropoxy-isophthalamide**, whereas the triplicate chemical compound name is **N1,N3-Bis-1,3-benzodioxol-5-ylmethyl-4-ethoxy-isophthalamide** . The examiner recommends to remove any extra same compound name. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 3, 6, and 20 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claim sets forth the treatment of breast cancer. However, the specification never has shown the actual experimental data for treating the breast cancer, but has disclosed the mechanistic nature of inhibiting matrix metalloproteinase enzymes so that one of the diseases, such as, the breast cancer might be treated indirectly. There are many reasons why the breast cancer might arise from a wide variety of sources, such as viruses (e.g. EBV, HHV-8, and HTLV-1), exposure to chemicals such as tobacco tars, genetic disorders, ionizing radiation, and a wide variety of failures of the body's cell growth regulatory mechanisms.

The specification falls short because data essential for how the breast cancer can be treated by means of inhibiting matrix metalloproteinase enzymes is not described in the specification.

In *In re Wands*, 8 USPQ2d 1400 (1988), factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. § 112, first paragraph, have been described. They are:

1. the nature of the invention,
2. the state of the prior art,
3. the predictability or lack thereof in the art,

4. the amount of direction or guidance present,
5. the presence or absence of working examples,
6. the breadth of the claims,
7. the quantity of experimentation needed, and
8. the level of the skill in the art.

The Nature of the Invention

The nature of the invention in claims 3, 6, and 20 is the method of treating breast cacinoma by administering to a patient the compound of formulas III and VI.

The State of the Prior Art

The state of the prior art is that according to US Patent No. 5,948,780, MMP inhibitors have been used to prevent and treat congestive heart failure and other cardiovascular diseases. Recent data has revealed that specific enzymes are closely related to some diseases ,while there is no effect on other diseases. The MMPs are generally classified based on their substrate specificity; particularly , the collagenase subfamily of MMP-1, MMP-8, and MMP-13 selectively cleave interstitial collagen tissue. This has been noticed by the discovery that only MMP-13 is over-expressed in breast carcinoma, whereas MMP-1 alone is over-expressed in papillary carcinoma (see Chen et al., J. Am .Chem. Soc., 2000;122;9648-9654). Furthermore, according to Wo/01/63244A1 and US Patent No. 6,008,243, few selective inhibitors of MMP-13 have been approved: however, there is no conclusive indicator that the selective or nonselective inhibitor of MMP-13 has been approved for treating the breast cancer.

The predictability or lack thereof in the art

The instant claimed invention is highly unpredictable as discussed below:

It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. In re Fisher, 427 F.2d 833, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. In the instant case, the instant claimed invention is highly unpredictable since one skilled in the art would recognize that inhibiting the MMPs would result in only the specific site of the interstitial collagen tissue; this kind of treatment can not be translated to the possible treatment of breast cancer in regards to their therapeutic effects.

Hence, in the absence of a showing of correlation between breast cancer claimed as capable of treatment by the compounds of formulas III and VI and the inhibition of matrix metalloproteinase, one of skill in the art is unable to fully predict possible results from the administration of the claimed compounds of formulas III, and VI due to the unpredictability of the role of inhibiting the MMPs, i.e. whether promotion or inhibition would be beneficial for the treatment of the breast cancer.

The nature of pharmaceutical arts is that it involves screening *in vitro* and *in vivo* to determine which compounds exhibit the desired pharmacological activities. There is no absolute predictability even in view of the seemingly high level of skill in the art. The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic regimen on its face.

The amount of direction or guidance present

The direction present in the instant specification is that the compounds of formulas III and VI can inhibit the the MMPs which helps in the treatment for breast carcinoma. However, the specification is silent and fails to provide guidance as to whether the breast carcinoma listed (pages 53 and 55) requires the inhibition of the MMPs for treatment, i.e. the specification fails to provide a correlation between the disease listed and the inhibition of the MMPs. Also, there is no direction and guidance for the inhibition of the MMPs for the treatment of the breast cancer.

The presence or absence of working examples

There is no working example for the treatment of breast carcinoma, rheumatoid arthritis, osteoarthritis, inflammation, or a heart failure. Furthermore, there are not other working examples for any other diseases listed in the specification. Also, the compounds which are discloses in the specification have no pharmacological data regarding the treatment of any other disease besides inhibitory activity of various MMPs using compounds from various classes and have no data on the possible treatment of the various diseases that require the inhibitory activity of various MMPs. Also, the specification fails to provide working examples as to how the listed diseases can be treated by the inhibition of various MMPs, i.e. again, there is no correlation between the diseases listed and inhibition of various MMPs.

The breadth of the claims

The breadth of the claims is that the compounds of formulas III and VI can treat the breast cancer by the inhibition of the MMPs , without regards as to the affect of the inhibition of the MMPs on the stated disease.

The quantity of experimentation needed

The quantity of experimentation needed is undue experimentation. One of skill in the art would need to determine what listed diseases would be benefited by the inhibition of the MMPs and would furthermore then have to determine whether the claimed compounds would provide treatment of the disease by the inhibition of the MMPs.

The level of the skill in the art

The level of skill in the art is high. However, due to the unpredictability in the pharmaceutical art, it is noted that each embodiment of the invention is required to be individually assessed for physiological activity by in vitro and in vivo screening to determine which compounds exhibit the desired pharmacological activity and which diseases would benefit from this activity.

Thus, the specification fails to provide sufficient support of the broad use of the compounds of formulas III and VI for the treatment of the breast cancer by the inhibition of the MMPs. As a result, necessitating one of skill to perform an exhaustive search for which the breast cancer can be treated by the compounds of formulas III and VI in order to practice the claimed invention.

Genentech Inc. v. Novo Nordisk A/S (CA FC) 42 USPQ2d 1001 , states that " a patent is not a hunting license. It is not a reward for search , but compensation for its successful conclusion" and "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable".

Therefore, in view of the Wands factors and In re Fisher (CCPA 1970) discussed above, to practice the claimed invention herein, a person of skill in the art would have to engage in undue experimentation to test which diseases can be treated by the compound encompassed in the instant claims, with no assurance of success.

Claims 3 and 18-23 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claims 3 and 18, the chemical symbols " R^4R^5—N " and " N —R^4R^5 " are recited. The expression of the bond "— " between the N and the R^4R^5 is vague and indefinite because the chemical symbols can be interpreted in two ways: the R^4 and the R^5 groups of R^4R^5—N are connected to each other side-by-side, or the R^4 and the R^5 groups are attached separately to the nitrogen atom.

Therefore, Appropriate correction is required.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Taylor Victor Oh whose telephone number is 571-272-0689. The examiner can normally be reached on 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

*** 12/3-04

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